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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/031,819	08/12/2002	Ronald Vale	UCSD-06783	1389

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EXAMINER	
SHIBUYA, MARK LANCE	

ART UNIT	PAPER NUMBER
1639	

DATE MAILED: 12/20/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/031,819	VALE ET AL.	
	Examiner	Art Unit	
	Mark L. Shibuya	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 August 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-69* is/are pending in the application.

4a) Of the above claim(s) *1-36 and 40-69* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37-39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/31/03 & 8/17/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-69 are pending. Claims 1-36 and 40-69 are withdrawn. Claims 37-39 are examined.

Election/Restrictions

2. Applicant's election with traverse of Group III (claims 37-40) in the reply filed on 7/8/2005 is acknowledged. The traversal is on the ground(s) that the requirement that the Groups be further restricted is not proper because the claims of Group III do not lack a special technical feature over the reference of WO 94/08041 (of record and as cited in the Requirement for Election/Restriction, mailed 5/4/2005). Upon further consideration, this requirement for a further election of a pairwise combination for Group III is withdrawn. However, the elected claims are rejected over the prior art (see below). Applicant did not appear to traverse the restriction requirement among Groups I-III. Applicant's election of species that are components of the microtubule system, ATPase assays, and test compounds is acknowledged.

3. Claims 1-36 and 40-69 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Invention and species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 7/8/2005. Claim 40, drawn to components of a cytoskeletal system that is an actin/myosin system, is not considered to read upon the

elected species of components of a microtubule system, and is therefore withdrawn from consideration.

Priority

4. This application is the national stage of PCT/US98/18368, filed 9/3/1998, (see WO 99/11814), which claims benefit of 60/057,895, filed 9/4/1997.

5. The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Provisional Application No. 60/057,895, filed 9/4/1997, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. Provisional Application No. 60/057,895, filed 9/4/1997, does not disclose detecting a change in coupling between ATP hydrolysis and force generation, wherein said change indicates that a compound modulates activity of a cytoskeletal system (as in clam 37). Therefore, priority is granted only to the international filing date of PCT/US98/18368, filed 9/3/1998.

Information Disclosure Statement

6. The Information Disclosure Statement (IDS), entered 3/31/2003, fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein regarding reference 38, has not been considered.

7. The Information Disclosure Statement (IDS), entered 8/17/2005, has been considered.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 37-39 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This rejection is for lack of written description.

Vas-Cath Inc. v. Mahurkar, 19 USPQ 2d 1111, 1117, states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought,

he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." The instant specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

The specification does not disclose a representative number of species of the encompassed genera of all cytoskeletal systems, and methods of identifying a therapeutic lead compound that modulates the activity of any cytoskeletal system, wherein detecting a change in coupling between ATP hydrolysis and force generation indicates that said compound modulates activity of a cytoskeletal system, so that the skilled artisan cannot envision the detailed component structures of any and all such cytoskeletal systems, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. The instant disclosure states: "The number and identity of cytoskeleton components that have been identified thus far are legion, and far too numerous to be completely listed here." The specification provides one example of such an assay procedure as per claim 37, wherein compounds from the marine sponge *Adocia sp.* inhibit the kinesin ATPase motor and its relationship to microtubules (see Example 3 of the instant specification). Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, at 1483 (finding claims directed

to *mammalian* FGF's were found to be unpatentable due to lack of written description for that broad class, where the specification provided only the *bovine* sequence).

Therefore, only the kinesin ATPase motor and the microtubule component system and assay, as taught by the instant specification, but not the full breadth of the claim, meets the written description provision of 35 U.S.C. § 112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. § 112 is severable from its enablement provision (see page 1115).

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 37-40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 37 recites the limitation "a cytoskeletal system" in lines 3, 4, 9. There are uncertain antecedent bases for these limitations in the claim, because the relationship of these limitations to the term "a cytoskeletal system", in line 2, is unclear.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

10. Claims 37-39 are rejected under 35 U.S.C. 102(e) as being anticipated by Goldstein et al., US 6,207,403 B1.

The claims are drawn to methods of identifying a therapeutic lead compound that modulates activity of a cytoskeletal system, said method comprising: i) providing an assay mixture comprising a first component of a cytoskeletal system and a second component of a cytoskeletal system, wherein said first component and said second component specifically bind to each other; ii) contacting said assay mixture with a test compound to be screened for the ability to inhibit or enhance binding between said first component and said second component; iii) detecting a change in coupling between ATP hydrolysis and force generation; wherein said change indicates that said compound modulates activity of a cytoskeletal system.

Goldstein et al., US 6,207,403 B1, throughout the patent and the claims, discloses and claims methods of identifying a therapeutic lead compound (col. 2) that specifically modulates (e.g., inhibits) a kinesin "molecular motor" (col.s 3-4) binding activity to microtubules, which reads on inhibiting a cytoskeletal system, said method comprising: i) providing an assay mixture comprising a first kinesin motor, reading on a component of a cytoskeletal system, and microtubules, reading on a second

microtubule component of a cytoskeletal system, (as in claims 38 and 39), wherein said first component and said second component specifically bind to each other; (see e.g., claim 1 of the '403 patent); ii) contacting said assay mixture with test compounds (at col. 4) derived from a marine sponge, Haliclona (also known as Adocia) sp., reading on test compounds to be screened for the ability to inhibit or enhance binding between said first component (kinesin motor) and said second component (microtubules); iii) assaying for inhibition at a kinesin ATPase site (col. 5), and inhibition at a microtubule binding site, (see claims 1 and 2 of the '403 patent), reading on detecting a change in coupling between ATP hydrolysis and force generation (col. 17, lines 18-49 and Table 2 (cf. Table 2 at p. 50 of the instant application)); wherein said change indicates that said compound modulates activity of a cytoskeletal system (see e.g., claim 1 of the '403 patent).

11. Claims 37-39 rejected under 35 U.S.C. 102(a) as being anticipated by Sakowicz et al., (10 April 1998) Science Vol. 280, pp. 292-295.

Sakowicz et al., (10 April 1998) Science Vol. 280, pp. 292-295, throughout the publication, discloses methods of identifying a therapeutic lead compound (p. 295) that specifically modulates (e.g., inhibits) a kinesin "molecular motor" (see, e.g., abstract) activity, which reads on inhibiting a cytoskeletal system, said method comprising: i) providing an assay mixture comprising a first kinesin motor, reading on a component of a cytoskeletal system, and microtubules, reading on a second microtubule component of a cytoskeletal system, (as in claims 38 and 39), wherein said first component and

said second component specifically bind to each other; (p. 293, col. 1); ii) contacting said assay mixture with test compounds (p. 293, Figure 1) derived from a marine sponge, Haliclona (also known as Adocia) sp., reading on test compounds to be screened for the ability to inhibit or enhance binding between said first component (kinesin motor) and said second component (microtubules); iii) assaying for inhibition at a kinesin ATPase site (p. 293, Figure 2, and Table 1 (cf. Table 2 at p. 50 of the instant application)), and inhibition at a microtubule binding site, (pp. 293-94, bridging paragraph), reading on detecting a change in coupling between ATP hydrolysis and force generation (p. 293, col. 1); wherein said change indicates that said compound modulates activity of a cytoskeletal system (pp. 293-94, bridging paragraph).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

12. Claims 37-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Stewart et al.**, (June 1993) Proc. Natl. Acad. Sci. USA, Vol. 90, pp. 5209-5213 and **Ashby et al., US 5,569,588** (10/96), (IDS entered 3/31/2003, reference no. 26).

The claims are drawn to methods of identifying a therapeutic lead compound that modulates activity of a cytoskeletal system, said method comprising: i) providing an assay mixture comprising a first component of a cytoskeletal system and a second component of a cytoskeletal system, wherein said first component and said second component specifically bind to each other; ii) contacting said assay mixture with a test compound to be screened for the ability to inhibit or enhance binding between said first component and said second component; iii) detecting a change in coupling between ATP hydrolysis and force generation; wherein said change indicates that said compound modulates activity of a cytoskeletal system.

Stewart et al., throughout the publication, teach methods of modulating the activity of a cytoskeletal system, said method comprising: i) providing an assay mixture comprising the kinesin or *ncd* (non-claret disjunctional) gene product, (see, e.g., abstract), reading on a first component of a cytoskeletal system and a microtubules, reading second component of a cytoskeletal system, (p. 5210, para 3-4, Motility Assays) wherein said first component and said second component specifically bind to each other, (p. 5209, para 1); and detecting a change in coupling between ATP hydrolysis

and force generation (see p. 5210, para 3-5, p. 5212, Figures 1-2); wherein said change indicates that said compound modulates activity of a cytoskeletal system (p. 5213, para 2). Stewart et al. disclose the use of the drug taxol in preparing the microtubules (p. 5210).

Stewart et al., does not disclose using the methods of modulating the activity of a cytoskeletal system to identify a therapeutic lead compound.

Ashby et al., US 5,569,588 (IDS entered 3/31/2003, reference no. 26), throughout the patent and especially at col. 4, lines 1-12, teach that new compounds which interfere with tubulin-based cytoskeletal elements, such as taxol, would provide candidates for taxol-like pharmaceuticals.

It would have been *prima facie* obvious, at the time the invention was made, for one of ordinary skill in the art to have made and used methods of modulating the activity of a cytoskeletal system, as taught by Stewart et al., to identify a therapeutic lead compound, as taught by Ashby et al.

One of ordinary skill in the art would have been motivated to make and use methods of identifying compounds because Ashby et al. teach that new compounds that interfere with tubulin-based cytoskeletal element, may provide candidate taxol-like pharmaceuticals; and because Stewart et al., teach assays for assessing modulation of the activity of kinesin or ncd gene product in a cytoskeletal system, and because Stewart uses taxol in preparing microtubules as a component in their assay.

One of ordinary skill in the art would have had a reasonable expectation of success in making and using methods of modulating the activity of a cytoskeletal

system, because detection of changes in coupling between ATP hydrolysis and force generation of components of a cytoskeletal system, wherein said changes indicate modulation of the activity of a cytoskeletal system, was known in the art, as taught by Stewart et al., and because inhibitors of microtubule cytoskeletal systems, such as taxol, also were known in the art, as taught by Ashby et al.

Conclusion

13. Claims 37-39 are rejected. Claim 40 is withdrawn.

14. The art made of record and not relied upon is considered pertinent to applicant's disclosure. Hopkins et al., (February 2000), Inhibitors of Kinesin Activity from Structure-Based Computer Screening, Biochemistry, Vol. 39, pp. 2805-14.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Mark L. Shibuya whose telephone number is (571) 272-0806. The examiner can normally be reached on M-F, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571) 272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Mark L. Shibuya
Examiner
Art Unit 1639

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